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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/536,800

01/17/2006

William Levine

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01/05/2010

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EXAMINER

CHEN, CATHERYNE

ART UNIT

PAPER NUMBER

1655

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DELIVERY MODE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/536,800	Applicant(s) LEVINE ET AL.	
	Examiner CATHERYNE CHEN	Art Unit 1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Sept. 18, 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3 and 5-16 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 5-16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The Amendments filed on Sept. 18, 2009 has been received and entered.

Currently, Claims 1-3, 5-16 are pending. Claims 1-3, 5-16 are examined on the merits. Claim 4 is canceled.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restrictions

Applicant's election without traverse of Sambucus nigra, Centella asiatica, Enchinacea purpurea in the reply filed on Dec. 15, 2006 is acknowledged.

Response to Arguments

Claim Rejections - 35 USC § 103

Claims 1-3, 8-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mathiowitz et al. (US 6217908 B1)), 1001herbs (<http://www.1001herbs.com/elderberrycombo/>), Holistic-online (<http://www.holistic-online.com/herbal-med/Herbs/h18.htm>), Ceschel et al. (2001, Drug Delivery, 8, 161-171) for the reasons set forth in the previous Office Action, which is set forth below. All of Applicant's arguments regarding this ground of rejection have been fully considered but are not persuasive.

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Mathiowitz et al. teaches composition as drug delivery systems in the area of gastrointestinal, vaginal, and respiratory drug delivery, administration via nasal or oral passage (column 1, lines 11-17). Controlled release systems for drug delivery by adhering the lining of the appropriate viscus, its content can be delivered to the target tissues as a function of proximity and duration of contact (column 1, lines 21-29). Mucoadhesion improves bioavailability (column 1, lines 53-58). Bioadhesive polymers in the form of or as a coating on microcapsules containing drugs or bioactive substance (column 3, lines 56-57). Two classes of polymers are useful for its bioadhesive properties are polyacrylic acid (column 7, lines 22-25), natural polymer is polyvinylpyrrolidone and synthetically modified natural polymer is hydroxypropyl cellulose (column 7, lines 51, 57). Lectins from *Sambucus nigra* can be covalently attached to microspheres to render them target specific to the mucin and mucosal cell layer (column 11, lines 1-15). The microspheres are administered in suspension to mucosal membranes via the nose, mouth, rectum or vagina with pharmaceutically acceptable carriers for oral administration that are compatible with the polymeric material (column 14, lines 43-46). The non-adhesive side would be intrinsically taught because the inside of the shell would be in contact with the dispersing agent; thus, the dispersing agent would be the non-adhesive side.

However, it does not teach *Echinacea purpurea*, *Centella asiatica*, lactose, contact time.

1001herbs teaches Echinacea purpurea and elderberry or Sambucus nigra at 394 mg for use in boosting immune system to prevent cold-and-flu (paragraph 1).

Holistic-online teaches Centella asiatica or gotu kola for treating fever, immune system strengthening (page 2, Useful for) and infections (page 2, paragraph 2).

Ceschel et al. teaches a variety of drugs can be absorbed by buccal, sublingual or gingival mucosa and local treatment of inflammatory disease at the site of administration and the degrees of systemic side effects can be minimized (page 161, right column, paragraph 1). The formulation is for a mucoadhesive, specifically buccal, administration likes lozenges, troches, gels, oral rinse or mouthwash for delivery of drugs through the mucosa of the oral cavity (page 161, paragraph 2). Bioadhesive polymers-copolymers can control drug delivery by localizing in a specific surface which is able to absorb drugs, leading to enhancement of bioavailability, prolonging residence time and ensuring optimal contact with the absorbing surface and have gelling properties that can be exploited to obtain a control of drug release (page 162, left column, lines 2-9). Composition for tablets with lactose at amounts of 42.17, 37.17, 32.17%, mucoadhesive PVP (polyvinylpyrrolidone) PK30 at amounts of 10, 20, 30% (page 162, Table 1). Table 8 shows tablet detachment or disgregation time at 1 hour 24 minutes. The concentration of mucoadhesive polymer need to be more than 10% to avoid tablet detachment and that disgregation time increased with an increase of mucoadhesive concentration (page 170, paragraph 1).

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Mathiowitz et al. teaches composition as drug delivery systems with lectin, a plant extract from *Sambucus nigra*. The drug delivery of Mathiowitz et al. can be used to deliver the 1001 herbs taught *Echinacea purpurea* and elderberry or *Sambucus nigra* at 394 mg for use in boosting immune system (paragraph 1) and Holistic-online taught *Centella asiatica* or gotu kola for treating fever, immune system strengthening (page 2, Useful for) and infections (page 2, paragraph 2). Thus, an artisan of ordinary skill would reasonably expect that ingredients that can boost immune system could be used as the type composition for delivery taught by the references. This reasonable expectation of success would motivate the artisan to use *Sambucus nigra*, *Centella asiatica* and *Echinacea purpurea* as the muco-adhesive drug in the reference composition. Thus, using *Sambucus nigra*, *Centella asiatica* and *Echinacea purpurea* as the muco-adhesive drug is considered an obvious modification of the references.

Mathiowitz et al. teaches bioadhesive polymers in the form of or as a coating on microcapsules containing drugs or bioactive substance (column 3, lines 56-57). Ceschel et al. teaches mucoadhesive, specifically buccal, administration likes lozenges, troches, gels, oral rinse or mouthwash for delivery of drugs through the mucosa of the oral cavity (page 161, paragraph 2) and composition for tablets with lactose at amounts of 42.17, 37.17, 32.17%, mucoadhesive PVP (polyvinylpyrrolidone) PK30 at amounts of 10, 20, 30% (page 162, Table 1) with Table 8 showing tablet detachment or disgregation time at 1 hour 24 minutes. Thus, it would be obvious to add lactose into mucoadhesive formulation, such as that taught by Ceschel et al. An artisan of ordinary skill

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would clearly expect that the bioadhesive tablets taught by Ceschel et al. would function successfully to administer the bioadhesive microcapsules taught by Mathiowitz et al. This reasonable expectation of success would motivate the artisan to modify Mathiowitz et al. to include lactose as an effective means to administer the bioadhesive formulation.

The references do not specifically teach adding the ingredients in the amounts claimed by applicant. However, the references do teach the composition for mucoadhesive compositions. Ceschel et al. teaches composition for tablets with lactose at amounts of 42.17, 37.17, 32.17%, mucoadhesive PVP (polyvinylpyrrolidone) PK30 at amounts of 10, 20, 30% (page 162, Table 1). Table 8 shows tablet detachment or disgregation time at 1 hour 24 minutes. The concentration of mucoadhesive polymer need to be more than 10% to avoid tablet detachment and that disgregation time increased with an increase of mucoadhesive concentration (page 170, paragraph 1). The amount of a specific ingredient in a composition that is used for a particular purpose (the composition itself or that particular ingredient) is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Thus, optimization of general conditions is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient to add in order to best

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achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization of ingredient amount would have been obvious at the time of applicant's invention.

Applicant argues that the references 1001herbs (<http://www.1001herbs.com/elderberrycombo/>) and Holistic-online (<http://www.holistic-online.com/herbal-med/Herbs/h18.htm>) are not prior art.

In response to Applicant's argument, 1001herbs can go back to an internet date of 1998, see (<http://web.archive.org/web/19981207055325/http://1001herbs.com/elderberrycombo/>), and the reference does teach that elderberry extract is used in immune system (page 1). Thus, 1001herbs is prior art. Holistic-online teaches that Gotu Kola, which is *Centella asiatica* has been used in India for thousands of years for treating fever (see History, pages 1-2). Thus, knowledge that *Centella asiatica* is used for a specific purpose is known before the prior art date.

Applicant argues that the references do not teach muco-adhesive abilities of the composition.

In response to Applicant's argument, Mathiowitz et al. teaches composition as drug delivery systems in the area of gastrointestinal, vaginal, and respiratory drug delivery, administration via nasal or oral passage (column 1, lines 11-17). These areas are mucosal tissues. It further teaches that controlled release systems for drug delivery by adhering the lining of the appropriate viscus, its content can be delivered to the target tissues as a function of proximity and

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duration of contact (column 1, lines 21-29) and that mucoadhesion improves bioavailability (column 1, lines 53-58). Bioadhesive polymers in the form of or as a coating on microcapsules containing drugs or bioactive substance (column 3, lines 56-57). Two classes of polymers are useful for its bioadhesive properties are polyacrylic acid (column 7, lines 22-25), natural polymer is polyvinylpyrrolidone and synthetically modified natural polymer is hydroxypropyl cellulose (column 7, lines 51, 57). Lectins from *Sambucus nigra* can be covalently attached to microspheres to render them target specific to the mucin and mucosal cell layer (column 11, lines 1-15). The microspheres are administered in suspension to mucosal membranes via the nose, mouth, rectum or vagina with pharmaceutically acceptable carriers for oral administration that are compatible with the polymeric material (column 14, lines 43-46). The non-adhesive side would be intrinsically taught because the inside of the shell would be in contact with the dispersing agent; thus, the dispersing agent would be the non-adhesive side. Because the language of the claim is "comprising" the fact that other ingredients are taught does not teach away from the claim.

Applicant argues that *Sambucus nigra* is taught for another purpose by Mathiowitz.

In response to applicant's argument that *Sambucus nigra* is taught for another purpose, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

Applicant argues that there is picking and choosing of the ingredients from the reference Mathiowitz.

In response to Applicant's argument, while the reference might not teach a specific embodiment with the claimed ingredients, the reference does list these ingredients as being appropriate for combination into a pharmaceutical formula for mucoadhesion. As discussed in *KSR International Co. v. Teleflex Inc.*, 550 U.S.--, 82 USPQ2d 1385 (2007) it is considered obvious to combine prior art elements known to be used in equivalent fields of endeavor together into a single combination. The reference clearly shows that the claimed ingredients were known to be used in equivalent fields of endeavor; thus, it is considered obvious to combine them together.

Applicant argues that *Centella asiatica* and *Echinacea purpurea* are not taught to have mucoadhesive abilities.

In response to applicant's argument that *Centella asiatica* and *Echinacea purpurea* are not taught to have mucoadhesive abilities, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

Applicant argues that the polymeric microspheres taught by Mathiowitz are not used for mucosal membranes.

In response to Applicant's argument, Mathiowitz teaches a method of delivering a compound to a patient comprising administering to a mucosal

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membrane a drug within a microparticle having polymeric surface with adhesive force (Claim 1). Thus, mucoadhesion is taught.

Applicant argues that the limitation of tablet coated with non-adhesive material is not taught.

In response to Applicant's argument, Mathiowitz et al. teaches bioadhesive polymers in the form of or as a coating on microcapsules containing drugs or bioactive substance (column 3, lines 56-57). The coated side will be the adhesive, while the non-coated side will be the non-adhesive side. The inside of the shell would be in contact with the dispersing agent; thus, the dispersing agent would be the non-adhesive side. Ceschel et al. teaches mucoadhesive, specifically buccal, administration likes lozenges, troches, gels, oral rinse or mouthwash for delivery of drugs through the mucosa of the oral cavity (page 161, paragraph 2) and composition for tablets with lactose at amounts of 42.17, 37.17, 32.17%, mucoadhesive PVP (polyvinylpyrrolidone) PK30 at amounts of 10, 20, 30% (page 162, Table 1) with Table 8 showing tablet detachment or disgregation time at 1 hour 24 minutes. Thus, it would be obvious to add lactose into mucoadhesive formulation, such as that taught by Ceschel et al. An artisan of ordinary skill would clearly expect that the bioadhesive tablets taught by Ceschel et al. would function successfully to administer the bioadhesive microcapsules taught by Mathiowitz et al. This reasonable expectation of success would motivate the artisan to modify Mathiowitz et al. to include lactose as an effective means to administer the bioadhesive formulation.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CATHERYNE CHEN whose telephone number is (571)272-9947. The examiner can normally be reached on Monday to Friday, 9-5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Catheryne Chen
Examiner Art Unit 1655

/Michael V. Meller/

Primary Examiner, Art Unit 1655